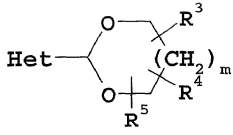
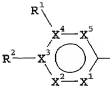
CLAIMS

1. A compound of formula (I):



(I)

wherein:-

Het is a five or six membered heteroaromatic ring of the formula  in which

one of R^1 and R^2 is optionally substituted heteroaryl and the other is optionally substituted heteroaryl or optionally substituted aryl; X^1 is a bond, X^3 and X^4 are each independently N or C and X^2 and X^5 are independently CH, N, NH, O or S; or X^3 and X^4 are C, one of X^1, X^2 and X^5 is N and the others are N or CH; but excluding compounds in which X^1 is a bond, one of X^2 and X^5 is N and the other is NH and X^3 and X^4 are both C;

R^3 is a group $-L^1-R^6$;

R^4 is hydrogen, alkyl or hydroxyalkyl; or

R^3 and R^4, when attached to the same carbon atom, may form with the said carbon atom a cycloalkyl, cycloalkenyl or heterocycloalkyl ring or a group $C=CH_2$;

R^5 is hydrogen or alkyl;

R^6 is hydrogen, alkyl, azido, hydroxy, alkoxy, aryl, arylalkyloxy, aryloxy, carboxy (or an acid bioisostere), cycloalkyl, cycloalkyloxy, heteroaryl, heteroarylalkyloxy, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, nitro, $-NY^1Y^2$, $-N(R^7)-C(=Z)-R^8$, $-N(R^7)-C(=Z)-L^2-R^9$, $-NH-C(=Z)-NH-R^8$, $-NH-C(=Z)-NH-L^2-R^9$, $-N(R^7)-SO_2-R^8$, $-N(R^7)-SO_2-L^2-R^9$, $-S(O)_nR^{10}$, $-C(=Z)-NY^1Y^2$ or $-C(=Z)-OR^{10}$;

R^7 is hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, or heterocycloalkyl;

R^8 is alkyl, alkoxy, aryl, arylalkyloxy, cycloalkyl, heteroaryl, heteroarylalkyloxy or heterocycloalkyl;

R^9 is alkoxy, aryl, arylalkyloxy, arylalkyloxycarbonylamino, carboxy (or an acid bioisostere), cycloalkyl, cyano, halo, heteroaryl, heteroarylalkoxy, heterocycloalkyl, hydroxy or $-NY^3Y^4$;

R^{10} is alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, or heterocycloalkyl;

L^1 represents a direct bond or a straight- or branched-chain alkylene linkage containing from 1 to 6 carbon atoms and optionally substituted by halogen, hydroxy, alkoxy or oxo;

L^2 is a straight- or branched-chain alkylene linkage containing from 1 to 6 carbon atoms;

Y^1 and Y^2 are independently hydrogen, alkenyl, alkynyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl or alkyl optionally substituted by alkoxy, aryl, cyano, cycloalkyl, heteroaryl, heterocycloalkyl, hydroxy, oxo, $-CO_2R^7$, $-CONY^3Y^4$ or $-NY^3Y^4$, or the group $-NY^1Y^2$ may form a 5-7 membered cyclic amine which (i) may be optionally substituted with one or more substituents selected from alkoxy, carboxamido, carboxy, hydroxy, oxo (or a 5, 6,or 7 membered cyclic acetal derivative thereof), alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl, or heterocycloalkyl or alkyl substituted by carboxy, carboxamido or hydroxy (ii) may also contain a further heteroatom selected from O, S, SO_2 or NY^5 and (iii) may also be fused to additional aryl, heteroaryl, heterocycloalkyl or cycloalkyl rings to form a bicyclic or tricyclic ring system;

Y^3 and Y^4 are independently hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkyl, cycloalkyl, heteroaryl or heteroarylalkyl, or the group $-NY^3Y^4$ may form a 5-7 membered cyclic amine as defined for $-NY^1Y^2$ above;

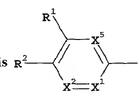
Y^5 is hydrogen, alkyl, aryl, arylalkyl, $-C(=Z)R^{10}$, $-C(=Z)OR^{10}$ or $-SO_2R^{10}$;

Z is an oxygen or sulphur atom;

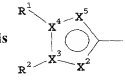
m is zero or an integer 1 or 2; and

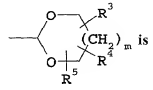
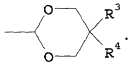
n is zero or an integer 1 or 2;

and N-oxides thereof, and their prodrugs; and pharmaceutically acceptable salts and solvates of compounds of formula (I) and N-oxides thereof, and their prodrugs.

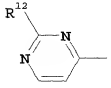
2. A compound according to Claim 1 in which Het is 

wherein one of X^1, X^2 and X^5 is N and the others independently are N or CH.

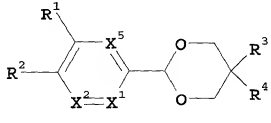
3. A compound according to Claim 1 in which Het is  wherein X^2 and X^5 are independently CH, N, NH, O or S, and X^3 and X^4 independently are N or C, but excluding compounds in which one of X^2 and X^5 is N and the other is NH and X^3 and X^4 are both C.

4. A compound according to Claim 1 in which the ring  is  .

5. A compound according to Claim 1 in which one of R^1 and R^2 is 4-pyridyl and the other is 4-fluorophenyl.

6. A compound according to Claim 1 in which one of R^1 and R^2 is 4-fluorophenyl and the other is  [wherein R^{12} is $R^{11}Z^2$- (in which R^{11} is alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, or alkyl substituted by alkoxy, aryl, cyano, cycloalkyl, heteroaryl, heterocycloalkyl, hydroxy, oxo, -CO_2R^7, -$CONY^3Y^4$ or-NY^1Y^2 and Z^2 is O or $S(O)_n$) or Y^1Y^2N- and Y^1 to Y^4, R^7 and n are as defined in Claim 1].

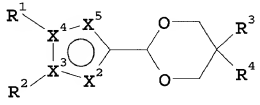
7. A compound according to Claim 1 having the formula (Ia)



(Ia)

in which R^3, R^4, X^1, X^2 and X^5 are as defined in Claim 1, one of R^1 and R^2 is 4-pyridyl and the other is 4-fluorophenyl, and N-oxides thereof, and their prodrugs; and pharmaceutically acceptable salts and solvates of compounds of formula (Ia) and N-oxides thereof, and their prodrugs.

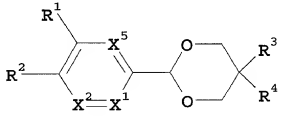
8. A compound according to Claim 1 having the formula(Ib)



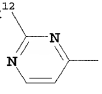
(Ib)

in which R^3, R^4, X^2, X^3, X^4 and X^5 are as defined defined in Claim 1, one of R^1 and R^2 is 4-pyridyl and the other is 4-fluorophenyl, and N-oxides thereof, and their prodrugs; and pharmaceutically acceptable salts and solvates of compounds of formula (Ib) and N-oxides thereof, and their prodrugs.

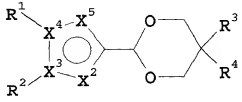
9. A compound according to Claim 1 having the formula (Ic)



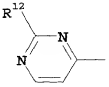
(Ic)

in which R^3, R^4, X^1, X^2 and X^5 are as defined in Claim 1, one of R^1 and R^2 is 4-fluorophenyl and the other is  [wherein R^{12} is Y^1Y^2N- in which Y^1 and Y^2 are as defined in Claim 1], and N-oxides thereof, and their prodrugs; and pharmaceutically acceptable salts and solvates of compounds of formula (Ic) and N-oxides thereof, and their prodrugs.

10. A compound according to Claim 1 having the formula (Id)



(Id)

in which R^3, R^4, X^2, X^3, X^4 and X^5 are as defined in Claim 1, one of R^1 and R^2 is 4-fluorophenyl and the other is  [wherein R^{12} is Y^1Y^2N- in which Y^1 and Y^2 are as defined in Claim 1], and N-oxides thereof, and their prodrugs; and pharmaceutically acceptable salts and solvates of compounds of formula (Id) and N-oxides thereof, and their prodrugs.

11. A compound according to Claim 1 in which R^3 and R^4 are both C_{1-4} alkyl groups.

12. A compound according to Claim 1 in which R^3 is -C(=O)-NY^1Y^2 (where Y^1 and Y^2 are as defined in Claim 1) and R^4 is C_{1-4}alkyl.

13. A compound according to Claim 12 in which Y^1 is hydrogen and Y^2 is alkyl or cycloalkyl.

14. A compound according to Claim 12 in which the group -NY^1Y^2 forms a 5-7 membered cyclic amine containing a further heteroatom selected from O and NY^5 (where Y^5 is H or alkyl).

15. A pharmaceutical composition comprising a compound according to Claim 1 together with a pharmaceutically acceptable carrier or excipient.

16. A pharmaceutical composition for use in the treatment of a condition which can be ameliorated by the administration of an inhibitor of TNF-alpha comprising an effective amount of a compound according to Claim 1.

17. A method for the treatment of a human or animal patient suffering from, or subject to, conditions which can be ameliorated by the administration of an inhibitor of TNF-alpha, which comprises the administration to said patient of an effective amount of a compound of claim 1.

18. A method according to Claim 17 for the treatment of asthma.

19. A method according to Claim 17 for the treatment of joint inflammation.

20. A compound substantially as hereinbefore described with reference to the Examples.